UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/624,530	07/24/2000	Richard Sackler	200.93185C2C	5659

23280 7590 08/11/2009

Davidson, Davidson & Kappel, LLC
485 7th Avenue
14th Floor
New York, NY 10018

EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
08/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/624,530	SACKLER ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8,13-16,24 and 27-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8,13-16,24 and 27-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/16/2009 has been entered.

Claim(s) 1-5, 9-12, 17-23, 25-26, 42-43 have been cancelled. Claim(s) 6, 24, 35, 37 has been amended. Claim(s) 6-8, 13-16, 24, 27-41 are pending and examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-8, 13, 24, 27-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 5,958,459. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims are drawn to a method

of treating pain comprising administering a composition comprising hydromorphone coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours, whereas the referenced claims are drawn to a composition comprising an opioid analgesic, hydromorphone, coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating pain with such composition since the main active agents is disclosed to be an opioid analgesic, which is a well known agent to treat pain in humans.

Claims 6-8, 13, 24, 27-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,143,322. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are an obvious variation of each other since both disclose a method of treating pain comprising administering a composition comprising hydromorphone coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours. It is noted that the same arguments regarding the limitations of the dissolution profile as well as the C_{max} and C_{24} values are also applied here.

Response to Arguments

Applicant's request to file a terminal disclaimer upon indication of allowable subject matter is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-8, 13-16, 24, 27-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldie et al. (US Patent 4,844,909) in view of Oshlack et al. (US Patent 5,286,493).

Goldie et al. teaches a solid release oral dosage form, the dosage form for the treatment of moderate to severe pain (col. 1) comprising a therapeutically effective amount of hydromorphone or salt thereof in a matrix wherein the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 mL aqueous buffer at pH 1.6 and 7.2 and at 37 °C overlaps with those as instantly claimed (Abstract). Peak plasma level is achieved between 2 and 4 hours (Abstract). The amount of hydromorphone released at a pH of

1.6 is less than 10% than that released at any pH up to 7.2 (col. 1, lines 29-35). Therapeutic levels of hydromorphone are maintained in vivo for *at least* 12 hours (col. 2, lines 3-10). Compositions wherein peak plasma levels are achieved between 4 and 8 hours are also taught to provide at least 12 hours of therapeutic effect (col. 2, lines 11-23). Gums, cellulose ethers, acrylic resins, C8-C50 long chain hydrocarbons, fatty acids, fatty alcohols, mineral oils, vegetable oils, waxes and polyalkylene glycols are disclosed as matrix materials (col. 2, line 47-col. 3, line 6). Dosage forms comprising between 2 and 40 mg of hydromorphone are taught (col. 2, lines 41-46). Blood plasma levels are exemplified as 1.0 ng/mL and 2.1 ng/mL at 12 hours and 1.1 ng/mL and 1.4 ng/mL at 24 hours (Tables 5 and 6). Goldie et al. also teach a dosage form comprising film-coated spheroids. The spheroids may contain water insoluble polymers, such as acrylic polymer and ethyl cellulose. The spheroids are film coated with a material that permits release of the active agent in a controlled rate. The film coat includes a water insoluble polymer, such as ethyl cellulose (col. 3, line 66 to col. 4, line 59). The examples also show that the coating is cured by way of exposure to heat of up to 50 and 60 °C.

Examiner notes that the limitations regarding "a dissolution profile which is substantially unaffected by exposure to storage conditions of at least a month at a temperature of 40 °C and a relative humidity of 75%" as well as C_{max} and C_{24} values are inherent when the same composition is cited by the prior art at the same dosage.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable

weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a dosage form wherein the peak plasma level is obtained between 4.4 and 8 hours, 4.6 and 8 hours, 4.8 and 8 hours, or 5.5 and 8 hours after administration of the dosage form because it is well known in the pharmaceutical art to have produced a formulation that gives a peak plasma level of the drug between 4 to 8 hours after administration. One would have been motivated to prepare a dosage form, which achieved maximum plasma levels between 4.4 to 8 hours to 5.5 to 8 hours because of an expectation of similar success in preparing a dosage form, which achieved therapeutic effects for at least 12 hours. Furthermore, even if between 2 and 4 hours is not considered inclusive of 4 hours, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize a dosage form with a the peak plasma level obtained between 4 and 8 hours after administration of the dosage form because Goldie et al. teaches that dosage forms achieving a peak plasma level between 2 and 4 hours are, surprisingly, interchangeable with dosage forms that achieve peak plasma levels between about 4 and 8 hours after administration. Both dosage forms are taught to achieve the desired effect. Namely, both are taught to

achieve a therapeutic effect for at least 12 hours. Accordingly, one would have been motivated to administer a dosage form that achieves a peak plasma level between 4 and 8 hours after administration because of an expectation of administering a dosage form suitable for achieving a therapeutic effect for at least 12 hours. It is noted that the exemplified clinical studies teach plasma levels at 24 hours wherein the amount present is a therapeutically effective amount because (1) the dosage form is taught to be therapeutically effective for at least 12 hours and the plasma levels at 24 hours are not significantly different than the plasma levels at 12 hours; and (2) the plasma levels are within the scope of the plasma levels as instantly claimed.

Goldie et al. teach as discussed above, however fail to specifically disclose a coating that has been stabilized by curing for about 24 hours or more at a temperature greater than the glass transition temperature of the hydrophobic polymer and at a relative humidity from about 60 to 100%.

Oshlack et al. teach that prior art curing of hydromorphone formulations have stability problems with respect to the controlled release dissolution profile (example 4). Oshlack et al. solves this problem by introducing a new method for obtaining a stabilized controlled release formulation by preparing a solid substrate comprising a therapeutically active agent, such as hydromorphone (col. 7, line 32), overcoating said substrate with a sufficient amount of a plasticized aqueous dispersion of an acrylic polymer, and then curing the coating substrate at a temperature above the glass transition temperature of the plasticized acrylic polymer, until the coated dosage form attains a stabilized dissolution profile substantially unaffected by exposure to storage

conditions of elevated temperature and/or elevated relative humidity (abstract and claims). Generally the curing time is about 24 hours or more (col. 8, lines 55-56). Furthermore, Oshlack et al. also teach that the substrate is overcoated with a barrier agent, to separate the therapeutically active agent from the acrylic coating (col. 7, lines 56-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the coating and curing process as taught by Oshlack et al. in the process of formulating the controlled release oral dosage formulation comprising hydromorphone for the method of treating pain as taught by Goldie et al.

One would have been motivated to use the coating curing process as taught by Oshlack et al. in the process of formulating the controlled release oral dosage formulation comprising hydromorphone for the method of treating pain as taught by Goldie et al. because: (1) both Oshlack and Goldie et al. teach controlled release oral dosage formulations comprising hydromorphone; (2) both Oshlack and Goldie et al. teach coatings that are cured; (3) Oshlack et al. teach that traditional curing has stability problems associated with the dissolution profile; (4) Oshlack et al. teach method of overcoming these stability problems by curing the coating substrate at a temperature above the glass transition temperature for over 24 hours, which provides a stabilized dissolution profile substantially unaffected by exposure to storage conditions of elevated temperature and/or elevated relative humidity. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in formulating a stabilized controlled release oral dosage form comprising hydromorphone, which possesses a

stabilized dissolution profile substantially unaffected by exposure to storage conditions of elevated temperature and/or elevated relative humidity.

Response to Arguments

Applicant argues that the Oshlack patent does not describe a curing "at a relative humidity from about 60 to 100%." To the contrary, it states that "it is not necessary to subject the coated substrate to humidity level above ambient conditions during the curing step in order to achieve a stabilized end product.

This is not persuasive because Oshlack does not teach that curing must be performed in humidity levels below ambient conditions. Oshlack merely mentions that it may not be necessary to do so. Nonetheless, the teachings of Oshlack still read on the limitation of relative humidity from about 60 to 100%, since ambient humidity is within the lower end of the claimed range. Applicant is reminded that all components of the claimed composition has been taught by the cited prior art references, therefore it is Applicant's burden to show factual evidence that the composition rendered obvious by the prior art does not possess the same properties as claimed.

It is respectfully pointed out that even though product-by-process claims are limited by and defined by the process; determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorp*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.

Cir. 1985). "The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

Applicant also argues that the combination of cited prior art references does not teach or suggest the specific release profiles because the compositions of the Goldie reference are different from the presently claimed compositions.

This is not persuasive because Applicant is again reminded that all components of the claimed composition has been taught by the cited prior art references, therefore all limitations drawn to specific release profiles are inherent. It is Applicant's burden to show factual evidence showing any differences in release profiles in a side-by-side comparison.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/
Primary Examiner, Art Unit 1617

YSC